REMARKS

I. Status of the Claims

1-194 are pending in the application. Claims 133-135 and 137-142 have been examined, as claims 1-132, 136 and 143-194 stand withdrawn pursuant to a restriction requirement and election of species. Claims 134 and 139-141 stand objected to, claims 133-135 and 137-142 stand rejected under 35 U.S.C. §112, first paragraph, claims 135 and 138-142 stand rejected under 35 U.S.C. §112, second paragraph, and claims 133-135 and 137-142 stand rejected under 35 U.S.C. §103 as obvious over U.S. Patent 5,689,562 in view of Dong *et al.*, U.S. Patent 6,224,882 and U.S. Patent 4,745,051. The specific grounds for rejection, and applicants' responses thereto, are set out in detail below.

II. Objections

The examiner has objected to claims 134 and 139-141 as containing non-elected species. Applicants submit that since the examiner is examining only the elected subject matter within these claims, the fact that they encompass non-elected subject matter is of no significance. Furthermore, should the elected species be found allowable, applicants will be entitled to examination of other species. Therefore, it is respectfully requested that this objection be held in abeyance until the examiner has had the opportunity to review applicants' response and amendments.

III. Rejection Under 35 U.S.C. §112, First Paragraph

Claims 133-135 and 137-142 stand rejected under the first paragraph of §112 as allegedly lacking an enabling disclosure. Applicants traverse the rejection, and will attempt to address

each of the issues raised by the examiner in the following discussion. Noted in this discussion is the acknowledgement that the following subject matter ***is*** enabled:

> A method of inhibiting cancer growth in a host having a cancer, said method comprising (a) isolating cancer cells from the host; (b) rendering said cancer cells inactive; and (c) reintroducing said inactivated cancer cells into said host in a pharmaceutical composition, said pharmaceutical composition further comprising an insect cell composition comprising insect cells containing a recombinant baculovirus vector encoding a β-interferon wherein said β-interferon is expressed in the insect cells.

This statement, coupled with other comments in the action, seem to suggest that the examiner takes issue with the following aspects of the present claims: (a) "treating" cancer; and (b) use of "any insect cell composition." With regard to the former, applicants note that "treating" and "inhibiting" do not seem to present distinct enablement issues. Treatments do ***not*** require eradication of cancers, and certainly one could argue that anything that "inhibits" a cancer also "treats" a cancer. Moreover, this term is found in the preamble and, hence, is not considered limiting. This said, applicants have amended the claims to recite "inhibiting" merely to advance the prosecution.

Turning the issue of insect cell compositions, applicants believe that β-interferon is not the only enabled immunomodulator. However, since the present prosecution is limited to examining the elected species - β-interferon - applicants need not comment on claims containing different immunomodulators, or claims that are generic in this respect.

The next insect cell issue appears to be that the examiner feels the compositions must contain baculovirus DNA. This is not understood. While one may advantageously use baculovirus-mediated expression of β-interferon, thereby resulting in a β-interferon containing insect cell composition that as a matter of course also contains a baculovirus expression construct, the examiner has not established why the claims should be so limited. As explained in

the specification, one may simply mix β-interferon with an insect cell composition, thereby obviating the need for any baculovirus expression construct. While the examiner makes numerous comments regarding what applicants do and do not show, there is no discussion about ***why*** a mixture of insect cells + β-interferon would not be expected to work in a manner similar to an insect cell composition that comprises β-interferon that was expressed in those cells.

It should be noted, in fact, that lyophilized cells are used in certain examples, thereby proving that intact cells are not required. In addition, applicants point out that the examiner admits later in the action that "insect cells ***whether genetically modified with a recombinant baculovirus expressing IFN-β or not, can function as an adjuvant*** ...." This would argue in favor of enablement for merely mixing IFN-β and insect cells, not against it.

The examiner also makes passing reference to routes of administration, but no further discussion is provided. Applicants note that various routes are exemplified, including subcutaneous and intratumoral injection. Again, applicants submit that the examiner has not explained why one could not take advantage of a variety of routes to achieve the goal of the present invention – to induce an anti-cancer immune response. Without such reasoning, a *prima facie* case of non-enablement will not stand.

In sum, and in light of the claims a presented for reconsideration, applicants respectfully submit that the present claims are enabled. Reconsideration and withdrawal of the rejection is requested.

IV. Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 135 and 138-142 stand rejected under the second paragraph of §112 as indefinite. Claim 135 is rejected for alleged lack of antecedent basis. Claim 138 is rejected for the phrase

"wherein said cancer is diffuse." Claims 139 is rejected for alleged lack of antecedent basis. Claim 135 has been canceled, and the rejections of claims 138 and 139 have been addressed by clarifying amendments. Reconsideration and withdrawal of the rejections is respectfully requested.

V. Rejection Under 35 U.S.C. §103

Claims 133-135 and 137-142 stand rejected under §103 as obvious over U.S. Patent 5,689,562 in view of Dong *et al.*, U.S. Patent 6,224,882 and U.S. Patent 4,745,051. Sobol is said to teach coadmininstration of cytokines – not including IFN-β - and tumor antigens. Dong is cited as teaching prostate tumor cells expressing IFN-β and the reduced metastasis and angiogenesis observed with these cells. Finally, the '882 and '051 patents are said to describe adjuvant effects of insect cells, optionally expressing IFN-β. From this, the examiner concludes that these references provide sufficient motivation to make and use the claimed invention. Applicants traverse.

First and foremost, it is the examiner's burden to establish a *prima facie* case of obviousness. There are three basic criteria that must be satisfied in order for any *prima facie* case to be proper: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations. *Manual of Patent Examining Procedure* §2142. See also *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed Cir. 1991). As all three elements must be found to establish a

prima facie case of obviousness, the absence of but a single element precludes a finding of obviousness.

Assuming *arguendo* that the third prong (each element in the prior art) is met, applicants submit that the other prongs are ***not*** met. In this regard, the examiner has failed to even ***comment*** on likelihood of success, and the rejection is therefore improper on its face. Moreover, as the examiner has acknowledged, "the physiological art is recognized as unpredictable," citing MPEP §2164.03. Office Action, page 6, bottom paragraph. Taken together, this admission and the absence of any discussion of likelihood of success renders the rejection fatally flawed.

Turning next to the motivation prong, applicants have considered the examiner's assertions in this regard, but find them wanting. First, it is quite notable that Sobol, the primary reference, ***fails to mention IFN-β, while listing numerous other molecules***. This is telling, and in light of the examiner's admission regarding "unpredictability" in the field, it runs counter to scientific principles to simply substitute the teachings of Sobol using IL-2 with IFN-β. Moreover, all of Sobol's claims and examples deal with use of ***viable*** (if non-proliferative) cells that express cytokines upon reintroduction into the host, leading one to the conclusion that the examiner found the use of isolated tumor antigens or inactive cells non-enabled. Thus, applicants submit that the Sobol patent fails to evince, to any degree, that the mere ***administration*** of IFN-β in conjunction with insect cells would be a useful endeavor.

Turning to the Dong reference, applicants certainly see the motivation in combining this article with Sobol, ***but again, only to the extent that Sobol discloses viable, non-insect cells that continue to produce IFN-β.*** There would be absolutely no motivation to combine Dong, which teaches the use of transformed prostate cancer cells expressing IFN-β, with aspects of Sobol that include non-viable host cells. Thus, in acknowledging the relationship of Sobol and Dong,

applicants submit that the are only related in a way ***that has nothing to do with the present invention – viable mammalian cells expressing cytokines***.

Finally, turning to the Smith patents, these references clearly are not combinable with Sobol and Dong for the simple reason that ***adjuvants and live cellular cancer vaccines would not be used together***. This is illustrated quite aptly by the fact that (a) Sobol and Dong fail to mention the words "adjuvant" or "insect cells," and (b) neither of the Smith patents mention transformed non-insect cells, the only common feature between Sobol and Dong Applicants cannot imagine a better example of how references ***fail completely to posit their own combination***, yet it is incumbent upon the examiner to find the suggestion to modify the primary reference ***in the prior art***. *In re Soli*, 137 USPQ 797 (CCPA 1963).[1] Thus, for this additional reason, applicants submit that the rejection is improper.

In sum, the examiner has identified references that individually might teach various elements of the claimed invention. However, the rejection is ***clearly*** based on an impermissible hindsight reconstruction of the invention as the references not only fail to posit their own combination, but actually suggest things other than what is now claimed. *In re Carroll*, 202 USPQ 571 (CCPA 1979) ("One of the more difficult aspects of resolving questions of non-obviousness is the necessity 'to guard against slipping into the use of hindsight.'"). As such, applicants submit that the rejection is improper; reconsideration and withdrawal is thus respectfully requested.

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1 "When, as in the instant case, the Patent Office finds, in the words of 35 U.S.C. §103, 'differences between the subject matter sought to be patented and the prior art,' it may not, without some basis in logic or scientific principle, merely alleged that such differences are either obvious or of no patentable significance and thereby force an [applicant] to prove conclusively that it is wrong." *Id.* at 187 USPQ at 801.

VI. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to that effect is earnestly solicited. Should the examiner have any questions regarding this response, a telephone call to the undersigned is invited.

Respectfully submitted,

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APPENDIX A: MARKED UP COPY OF AMENDED CLAIMS

133. (Amended) A method of [treating] inhibiting cancer comprising:

(a) isolating cancer cells from a host;

(b) rendering said cancer cells inactive;

(c) reintroducing said inactivated cancer cells into said host in a pharmaceutical composition, said pharmaceutical composition further comprising an insect cell composition.

138. (Amended) The method of claim 133, wherein said cancer is [diffuse] metastatic.

139. (Amended) The method of claim [133] 140, wherein said exogenous DNA is a baculovirus expression vector.

140. (Amended) The method of claim 139, wherein said [baculovirus expression vector further] insect cell composition comprises an exogenous [construct] DNA.

141. (Amended) The method of claim [140] 139, wherein said exogenous [construct] DNA encodes an immunomodulator.